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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/001,851	11/20/2001	Rachel E. Meyers	10147-56U1	1565

7590 02/13/2004

Intellectual Property Group
MILLENNIUM PHARMACEUTICALS, INC.
75 Sidney Street
Cambridge, MA 02139

EXAMINER	
SCHULTZ, JAMES	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 02/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/001,851	MEYERS ET AL.	
	Examiner	Art Unit	
	J. Douglas Schultz	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *27-31,34 and 35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27-31,34 and 35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *20 November 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/17/2003;10/15/2*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Election/Restrictions

1. Applicant's election without traverse of Group IX comprising claims 27-31, 34, and 35 each in part as drawn to SEQ ID NO: 2 in the paper entered November 17, 2003 is acknowledged.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 27, 31, and 34, and by dependency claims 28-30 and 35 recites the limitation "wherein the test compound is useful for modulating the phenomenon". There is insufficient antecedent basis for the term "phenomenon" in the claim.

4. Claims 27-31, 34, and 35 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: establishing that the compounds identified in the present methods that modulate 47169 activity also modulate tumorigenesis.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 27-31, 34 and 35 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants claims are directed to a method for assessing whether a test compound is useful for modulating tumorigenesis comprising adding a test compound to a test composition comprising the amino acid sequence at least 90% identical to, or a portion or fragment of, SEQ ID NO: 2 and that exhibits a 47169 activity, and comparing that to a control that contains no test compound.

The two elements of the above claims that necessitate this rejection is the language pertaining to a method of modulating tumorigenesis, and the language drawn to 90% identical, or a portion or fragment of SEQ ID NO: 2. Applicant is also referred to the Guidelines on Written Description published at FR 66(4) 1099-1111 (January 5, 2001) (also available at www.uspto.gov). The following passage is particularly relevant.

> The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within a genus, one must describe a sufficient number of species to reflect the variation within the genus. What constitutes a "representative number" is an inverse function of the skill and knowledge in the art. Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. In an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus.

In regards to tumorigenesis, the specification mentions that expression of 47169 is enhanced in lung (2-15x), breast (2-30x), and colon (2-10x) tumor tissues, relative to the corresponding non-tumorous tissues. The specification also asserts that significantly higher levels of expression were also observed in ovarian and liver tumor samples, relative to the corresponding normal tissues. In contrast, the claims indicate that tumorigenesis is modulated by 47169 activity, which leads to the conclusion that any modulator of 47169 activity will thus modulate tumorigenesis. However, the examiner can find no data anywhere in the specification or the prior art that supports such a cause and effect relationship identifying tumorigenesis caused by 47169 activity as claimed by applicant. Applicants have provided no teaching of how any function of 47169 activity is responsible for or causes tumorigenesis, and the prior art appears to be silent on such a relationship. Therefore, because applicants specification does not describe methods of identifying modulators are not considered to be in possession of methods of modulating tumorigenesis comprising comprising screening for modulators of 47169 activity.

Furthermore, applicants are not considered to be in possession of polypeptides having 90% similarity to 47169. Such a genus is quite broad, as one of skill in the art would understand. The instantly claimed polypeptide is 603 amino acids long, which means that any polypeptide with 90% homology could be different at up to 60 different amino acids. With 20 different substitutable amino acid possible at each of 60 different locations, there are 60^{20} possible variations, a number that approaches Avogadro's number of 6.022×10^{23}. In order to be considered to be in possession of such a broad genus, applicants would need to describe a representative sample of species of the broad genus. Applicant has not described any other amino acid sequences that retain the alleged function of 47169, and have thus not met even a minimum

sample, let alone a representative sample. Because it is well-known in the art that amino acid changes of even 1 residue can fundamentally alter or disable the function of the protein, and because applicants have not taught any domains, regions, or individual amino acid structures that could be altered while retaining the function of modulating tumorigenesis, applicants are not considered to be in possession of the invention as broadly claimed. Since nucleotide substitutions over any region of a polynucleotide's length such that only 90% of its original sequence remains will almost certainly result in some embodiments with altered function, and since applicant has not provided description of how to use such altered polynucleotides, one skilled in the art would not know how to use the invention as broadly claimed.

7. Claims 27-31, 34, and 35 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

A description of the invention is given above.

The factors listed below have been considered in the analysis of enablement:

(A) The breadth of the claims;
(B) The nature of the invention;
(C) The state of the prior art;
(D) The level of one of ordinary skill;
(E) The level of predictability in the art;
(F) The amount of direction provided by the inventor;
(G) The existence of working examples; and
(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The specification as filed does not provide sufficient guidance or appropriate examples that would enable a skilled artisan to screen for modulators of tumorigenesis using the methodology described. The method steps as described do not indicate any relationship between finding a modulator of 47169 activity and the claimed result of modulating tumorigenesis. On its face, merely practicing the method steps would only lead to finding inhibitors of 47169 activity. In contrast, the claims stipulate that finding such an inhibitor will necessarily identify the inhibitor as also being an inhibitor of tumorigenesis. This connection between inhibitors of tumorigenesis and 47169 activity would only be made if 47169 activity was directly responsible for tumorigenesis, a connection which is unsubstantiated in the specification and undescribed in the prior art. Thus, one attempting to practice the invention based on the method steps provided could produce only unpredictable results at best, necessitating trial and error experimentation. Thus, although the specification prophetically considers and discloses general methodologies of using the claimed method to screen for inhibitors of tumorigenesis, such a disclosure would not be considered enabling since such a connection has been merely alleged in applicants specification, and because finding compounds that reduce tumorigenesis by identifying inhibitors of a protein that has not been demonstrated to cause tumors is considered highly unpredictable.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Donoho et al. (United States Patent Number 6,555,669 B2, particularly SEQ ID NO:43).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. Douglas Schultz whose telephone number is 571-272-0763. The examiner can normally be reached on 8:00-4:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on 703-308-0447. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

James Douglas Schultz, PhD

SEAN McGARRY
PRIMARY EXAMINER
1635